12-30-05

AF

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re United States Patent Application of:		**Docket No.:**	**4171-102 CIP**
Appellant:	**Jason C.H. SHIH**	**Examiner:**	**Zachariah LUCAS**
Serial No.:	**10/007,613**	**Art Group:**	**1648**
Date Filed:	**October 26, 2001**	**Confirm. No.:**	**4213**
Title:	**METHOD AND COMPOSITION FOR STERILIZING SURGICAL INSTRUMENTS**	**Customer No.:**	**23448**

EXPRESS MAIL CERTIFICATE

I hereby certify that I am mailing the attached documents to the Commissioner for Patents on the date specified, in an envelope addressed to Mail Stop Appeal Brief – Patents, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, and Express Mailed under the provisions of 37 CFR 1.10.

Karin Szypszak

Karin Szypszak

December 29, 2005
Date

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CORRECTED APPEAL BRIEF IN RESPONSE TO NOVEMBER 29, 2005 NOTIFICATION OF NON-COMPLIANT APPEAL BRIEF IN U. S. PATENT APPLICATION NO. 10/007,613

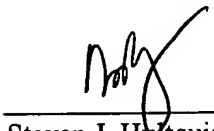
Mail Stop Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the November 29, 2005 Office Communication requesting a corrected Appeal Brief according to the rules set forth in 37 CFR 41.37, applicant submits the corrected Appeal Brief. Applicant has already submitted the required fee for entry of the Appeal Brief on January 3, 2005

and as such no additional fee is due.

Respectfully submitted,



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BRIEF ON APPEAL

Mail Stop Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is an appeal under 35 U.S.C. §134 from the Final Rejection in the Office Action dated June 30, 2004 Office Action, of claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 of U.S. Patent Application No. 10/007,613. This brief is submitted in response to the November 29, 2005 Notification of Non-Compliant Appeal Brief, and replaces the Appeal Brief filed on October 11, 2005 in this appeal.

No oral hearing is requested.

REAL PARTY IN INTEREST

The real party in interest in this appeal is BioResource International, Inc., the owner of the invention and patent rights of this application, by virtue of an Assignment of U.S. Patent Application No. 10/007,613 recorded in the assignment records of the U.S. Patent and Trademark Office on October 26, 2001 at reel 012366, frame 0566 (3 pages).

RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences known to Appellant, the Appellant's legal representative, or assignee, which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

STATUS OF CLAIMS

A complete listing of claims 1-83 of the present application is attached in the **Claim Appendix** hereof.

Withdrawn claims: 1-38, 68-69 and 75-79
Cancelled claims: 52, 57-61, 64-67, 70, 72, 81, 83
Objected claims: 39-51, 53-56, 63, 71, 73, 74, 80 and 82
Rejected claims: 39-51, 53-56, 63, 71, 73, 74, 80, and 82

Process claims 1-38 were withdrawn from consideration in response to a restriction requirement earlier in the prosecution of this application, and appellant has asserted the right to rejoin the withdrawn process claims 1-38 under MPEP §821.04 upon determination that the elected product claims are allowable.

Claims 68, 69, and 75-79 have been withdrawn from consideration as directed to non-elected species of proteolytic enzymes.

The examiner's objection to the claims 39-51, 53-56, 63, 71, 73, 74, 80 and 82 is that that such claims read on systems for treatment of articles that may be infected with prion proteins, wherein the systems are described as comprising the articles to be worked on.

Claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 have been finally rejected under 35 U.S.C. §103(a) by the Examiner in the June 30, 2004 Office Action, and such finally rejected claims are the subject of this appeal.

STATUS OF AMENDMENTS

A response was filed in the USPTO on August 30, 2004 to the June 30, 2004 Office Action finally rejecting claims 39-61, 63-65, 69, 71, 73-80 and 82 then pending in the application.

The response canceled claims 52, 57-61 and 64-65 and amended claims 39, 51, 53-56, 71, 80 and 82.

The response was entered by the examiner, as documented in the September 22, 2004 Advisory Action, in which the PTOL-303 form in paragraph 7 stated that the response "will be entered" and then related that "The status of the claims will be as follows: .... Claim(s) rejected: 35-51, 53-56, 63, 71, 73, 74, 80 and 82."

The Advisory Action confirmed that the August 30, 2004 response had overcome: the objection to the specification; the objection to claim 60; the rejection of claims 39-52, 56-61, 64 and 65 for scope of enablement regarding the temperature range that may be used for the sterilization of articles; the rejection of claim 64 for scope of enablement; and the rejection of claims 56, 59, 71, 73 and 74 for containing new matter.

The Advisory Action stated that the response did not place the application in condition for allowance because:

> "The amendments have not overcome the objection to the claims as reading on systems for treatment of articles that may be infected with prion proteins, wherein the systems are described as comprising the articles to be worked on. The Applicant has not responded to this objection other than to assert that the amendments to the claims have overcome the rejection. Because the claims still read on the systems, and describe the articles to be worked upon by the systems as part thereof, the objection is maintained."

The Advisory Action then stated that the amendments in the August 30, 2004 response had not overcome the rejections of claims on 35 USC 103(a) grounds, and concluded that "[T]he rejection is therefore maintained against pending claims 39-51, 53-56, 63, 71 and 73 for the reasons of record and the reasons above" [which have been quoted from the Advisory Action above].

SUMMARY OF THE CLAIMED SUBJECT MATTER

The present invention relates to systems and methods for disinfecting and sterilizing medical devices and like articles that are susceptible to contamination by infectious prion proteins, by combining thermal treatment and enzymatic degradation.

Specifically, the treated articles are heated to an elevated temperature and exposed to a proteolytic enzyme, either successively at two different durations or simultaneously.

The thermal treatment functions to render the infective prion protein proteolytically susceptible. The temperature for conducting such thermal treatment is below the pyrolytic destruction temperature of the infective prion protein, and preferably at least 40°C but not more than 150°C.

The enzymatic degradation uses a thermally stable proteolytic enzyme, such as keratinase or subtilisin, for reducing or degrading the infective prion protein, which has been rendered proteolytically susceptible by the thermal treatment. The temperature for conducting such enzymatic degradation is preferably from about 50°C to about 65°C.

Independent claim 39 recites a system comprising:

(a) one or more articles susceptible to contamination by infectious prion protein; (Page 4, lines 15-21; page 5, lines 1-19)

(b) means for heating said articles (no specific heating system is particularized);

(c) a proteolytic enzyme selected from the group consisting of keratinases and subtilisins (Page 6, lines 8-21) and

(d) means for exposing said articles to said proteolytic enzyme (page 7, lines 1-2 and page 14, Table 1), wherein said one or more articles are characterized by a first elevated temperature of at least 40°C and not more than about 150°C during a first duration (page 11, lines 1-4), wherein said articles are characterized by a second elevated temperature in a range of from about 50°C to about 65°C (page 6, lines 6)exposure to said proteolytic enzyme during a second, subsequent duration.

Independent claim 56 recites a system comprising:

(a) one or more articles susceptible to contamination by infectious prion protein (page 4, lines 15-21; page 5, lines 1-19; page 11, lines 5-16);

(b) means for heating said one or more articles (no specific heating device is particularized);

(c) a proteolytic enzyme selected from the group consisting of keratinases and subtilisins (page 6, lines 8-21); and

(d) means for exposing said articles to said proteolytic enzyme (page 7, lines 1-2 and page 14, Table 1), wherein said one or more articles are characterized by an elevated temperature of from about 40°C to about 60°C and exposure to said proteolytic enzyme (page 15, lines 16-17)

Independent claim 71 recites a system comprising

(a) a surgical instrument contaminated with infective prior protein (page 4, lines 15-21);

(b) means for heating the surgical instrument (no specific heater is particularized);

(c) a proteolytic enzyme (page 12, lines 18-21 and page 13, lines 1-2) that is thermally stable at a temperature in a range of from about 35°C to about 100°C and proteolytically effective to at least partially destroy the infective prion protein contaminating said surgical instrument (page 6, line 4, and page 12, lines 10-12);

(d) means for exposing the surgical instrument to the proteolytic enzyme (page 7, lines 1-2 and page 14, Table 1), wherein said surgical instrument is characterized by a first elevated temperature in a range of from about 100°C to about 150°C during a first duration (page 11, line 3), and wherein said surgical instrument is characterized by a second elevated temperature in a range of from about 35°C to about 100°C and exposure to said proteolytic enzyme during a second, subsequent duration (page 6,line 4).

Independent claim 80 recites a system comprising:

(a) one or more articles susceptible to contamination by infectious prion protein (page 4, lines 15-21 and page 5, lines 1-19);

(b) means for heating said articles (no specific heating apparatus is particularized);

(c) *Bacillus licheniformis* PWD-1 keratinase (page 13, lines 3-4); and

(d) means for exposing the heated articles to the *Bacillus licheniformis* PWD-1 keratinase (page 7, lines 1-2 and page 14, Table 1), wherein said articles are characterized by a first elevated temperature of at least 40°C and not more than about 150°C during a first duration (page 10, line 21 and page 11, lines 1-2), and wherein said articles are characterized by a second elevated temperature

in a range of from about 50°C to about 65°C and exposure to the *Bacillus licheniformis* PWD-1 keratinase during a second, subsequent duration (page 6, lines 3 and 6).

Independent claim 82 recites a system comprising:

(a) one or more articles susceptible to contamination by infectious prion protein (page 4, lines 15-21, page 5, lines 1-19 and page 11, lines 5-16);

(b) means for heating said articles (no specific heating device or system is particularized);

(c) *Bacillus licheniformis* PWD-1 keratinase (page 13, lines 3-4); and

(d) means for exposing the articles to *Bacillus licheniformis* PWD-1 keratinase (page 7, lines 1-2 and page 14, Table 1), wherein said articles are characterized by an elevated temperature of from about 40°C to about 60°C and exposure to the *Bacillus licheniformis* PWD-1 keratinase(page 15, lines 16-17).

GROUNDS OF OBJECTION/REJECTION TO BE REVIEWED ON APPEAL

The following references (copies of publications, not US Patents, in Evidence Appendix) were cited under 35 U.S.C. §103(a) in the June 30, 2004 Office Action finally rejecting the pending claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82:

(a) WHO Infection Control Guidelines for Transmissible Spongiform Encephalopathies: Report of a WHO Consultation, WORLD HEALTH ORGANIZATION (WHO), March 23-26, 1999 (hereinafter "WHO Document");

(b) **Huth** et al. U.S. Patent No. 6,448,062 (hereinafter "Huth");

(c) **Vlass** et al. U.S. Patent No. 6,210,639 (hereinafter "Vlass");

(d) **Potgeiter** et al. U.S. Statutory Invention Registration No. H1,818 (hereinafter "Potgeiter");

(e) **Shih** U.S. Patent No. 5,171,682 (hereinafter "Shih");

(f) **Bolton** et al., Molecular Characteristics of the Major Scrapie Prion Protein (hereinafter "Bolton"); and

(g) **Oesch** et al. Properties of the Scrapie Prion Protein: Quantitative Analysis of Protease Resistance (hereinafter "Oesch").

An Evidence Appendix is included herewith, including copies of the WHO Document, Bolton and Oesch, as well as an Affidavit under 37 CFR 1.132 filed on April 16, 2004 and entered into the record of this application.

Two grounds of objection/rejection are requested to be reviewed in this appeal:

(1) Whether it is appropriate for claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 to recite systems that include articles susceptible to contamination by infectious prion protein.

(2) Whether claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 are unpatentable under 35 U.S.C. §103(a) as being obvious over the WHO Document as the primary reference, in view of numerous secondary references including Huth, Vlass, Potgeiter, Shih, Bolton, and Oesch.

ARGUMENT

Ground of Objection No. (1): Whether it is appropriate for claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 to recite systems that include articles susceptible to contamination by infectious prion protein – Claim 39 is Representative

In the June 30, 2004 Office Action, the Examiner objected to claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82, on the ground that such claims were directed to systems for treating articles that may be infected with prion proteins, and that it is inappropriate for such claims to include the articles to be treated in the claimed systems for treating the articles.

In response to such objection, the Appellant amended claims 39 (from which claims 40-51, 53-55, and 63 depend), 56, 71 (from which claims 73 and 74 depend), 80 and 82 in the August 30, 2004 Response to recite a system that comprises one or more articles susceptible to contamination by infectious prion protein, means for heating such articles, a proteolytic enzyme, and means for exposing such articles to the proteolytic enzyme (see claims 39, 56, 71, 80, and 82).

As a result of such amendments, claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 are no longer limited to systems or apparatuses for treating prion-contaminated articles. Instead, they are now directed to a system that includes both the contaminated articles and means for treating such articles, and therefore overcome the Examiner's objections.

The Examiner's assertion in the September 22, 2004 Advisory Action that such amended claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 still read on system for the treatment of articles that may be infected by

prion proteins (see Advisory Action, page 2, second paragraph) is inconsistent with the claim language as amended in Appellents' August 30, 2004 Response and is incorrect.

Appellant therefore respectfully requests that the Board reverse the Examiner's objection to claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82.

Ground of Rejection No. (2): Whether claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 are unpatentable under 35 U.S.C. §103(a) as being obvious over the WHO Document as the primary reference, in view of numerous secondary references including Huth, Vlass, Potgeiter, Shih, Bolton, and Oesch – Claim 39 is Representative

Claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 stand rejected under 35 U.S.C. §103(a) as being obvious over the WHO Document as the primary reference, in view of numerous secondary references including Huth, Vlass, Potgeiter, Shih, Bolton, and Oesch.

This rejection is traversed because the Examiner failed to establish a *prima facie* case of obviousness to support such rejection.

The Office has the initial burden of showing a *prima facie* case of obviousness. *In re Bell*, 26 U.S.P.Q.2d 1529, 1530 (Fed. Cir. 1993). In order to properly establish a *prima facie* case of obviousness based on combination of several references, the Examiner must show a reason, suggestion, or motivation to lead an inventor to combine those references. *Pro-Mold and Tool Co. V. Great Lakes Plastics Inc.*, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996).

The representative claim 39 expressly requires:

"A system comprising:

(a) **one or more articles susceptible to contamination by infectious prion protein**;

(b) **means for heating said articles**;

(c) **a proteolytic enzyme selected from the group consisting of keratinases and subtilisins**; and

(d) **means for exposing said articles to said proteolytic enzyme**,

wherein said one or more articles are characterized by a first elevated temperature of at least

40°C and not more than about 150°C during a first duration, wherein **said articles are characterized by a second elevated temperature in a range of from about 50°C to about 65°C and exposure to said proteolytic enzyme during a second, subsequent duration**."

The language of claim 39 expressly requires that the prion-contaminated articles be "characterized by a second elevated temperature in a range of from about 50°C to about 65°C and exposure to said proteolytic enzyme during a second, subsequent duration."

Such express requirement in claim 39 further imposes an implicit structural limitation. Such system must provide a specific arrangement of the recited elements, i.e., the articles, the heating means, the proteolytic enzyme, and the exposing means, to enable simultaneous heating and enzymatic digestion of the prion-contaminated articles, so that the articles can be characterized by a second elevated temperature in a range of from about 50°C to about 65°C and exposure to the proteolytic enzyme during a second, subsequent duration, as required by claim 39.

The cited references, either taken singularly or in combination, do not provide any derivative basis for such specific arrangement of articles, heating means, proteolytic enzyme, and exposing means, to allow the prion-contaminated articles to be characterized by a second elevated temperature in a range of from about 50°C to about 65°C and exposure to the proteolytic enzyme during a second, subsequent duration, as expressly required by claim 39.

The primary reference cited by the Examiner, i.e., the WHO document, discloses sterilization of prion-contaminated surgical instruments by boiling or autoclaving with sodium hydroxide or sodium hypochlorite, followed by subsequent routine sterilization (see page 29, Appendix III, section 2 of the WTO document).

The Examiner conceded that the WHO Document does not teach usage of proteolytic enzyme for treating prion-contaminated articles, but attempted to remedy such deficiency of the WHO Document by combining teachings by various secondary references including Huth, Vlass, Potgeiter, Shih, Bolton, and/or Oesch about the use of proteolytic enzyme.

However, such hypothetical combination proposed by the Examiner only yields a system containing a mere aggregate of articles, heating means, proteolytic enzyme and exposing means, but it does not provide any derivative basis for a specific arrangement of such elements that enables simultaneous

heating and enzyme exposure of the prion-contaminated articles in such manner that such articles are characterized by a second elevated temperature in a range of from about 50°C to about 65°C and exposure to the proteolytic enzyme during a second, subsequent duration, as expressly required by claim 39 of the present application. In fact, none of the secondary references acknowledges, or even recognizes, the advantages of arranging the articles, the heating means, the proteolytic enzyme and the exposing means for simultaneous heating and enzyme exposure to allow the articles to be at an elevated temperature in a range of from about 50°C to about 65°C during exposure to a proteolytic enzyme.

In the September 22, 2004 Advisory Action, the Examiner asserted that claim 39 of the present application does not structurally distinguish over the cited prior art references, on the basis that there are no teachings demonstrating that the system suggested by the combination of the cited prior art references would not be capable of performing the functions of simultaneous heating and enzyme exposure.

However, it is clear that a specific arrangement of articles, heating elements, proteolytic enzyme, and exposing means is necessary for a system to perform the functions of simultaneous heating and exposing the articles to the proteolytic enzyme.

The system suggested by the combination of the cited prior art reference does not have such specific arrangement of articles, heating elements, proteolytic enzyme, and exposing means. Therefore, such prior art system is incapable of performing the functions of simultaneous heating and enzyme exposure.

Further, it has been well-established that when the claimed invention contains functional limitations not suggested by the prior art reference, the mere fact that the prior art could be so modified to perform such functions would not have made the modification obvious, unless the prior art suggested the desirability of the modification. See *In re Gordon*, 733 F.2d 900, 902, 221 UPSQ 1125, 1127 (Fed. Cir. 1984); see also *In re Mills*, 16 USPQ2d 1430 (CAFC 1990).

In this case, nothing in the cited references suggests the desirability of modifying the prior art system and re-arranging the prion-contaminated articles, the heating elements, the proteolytic enzyme, and the exposing means so as to allow simultaneous heating and enzyme exposure of the articles so that such articles are at elevated temperature in a range of from about 50°C to about 65°C during exposure to a proteolytic enzyme.

Therefore, claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 of the present application patentably

distinguish over all cited references.

It therefore is respectfully requested that the Board take cognizance of the absence of any proper basis of the §103 rejection of claim 39, as representative of appealed claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82, and correspondingly reverse the Examiner's rejection of such claims.

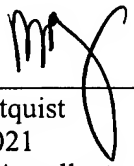
CONCLUSION

Based on the foregoing arguments and cited legal precedent, it is respectfully requested that the Board of Patent Appeals and Interferences reverse the decision of the Examiner finally rejecting claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 now pending in the application, consistent with the patentability of such claims over the cited art references.

No oral hearing is requested.

Inasmuch as this is a corrected Appeal Brief, responding to the Notification of Non-Compliant Appeal Brief, no additional fee is submitted to be due, since the Appeal Brief fee was paid on January 3, 2005. Nonetheless, if any fee or amount is determined to be properly payable, authorization hereby is given to charge any deficiency to Deposit Account No. 08-3284 of Intellectual Property/Technology Law.

Respectfully submitted,



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CLAIM APPENDIX

Appeal Claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 in a Listing of Claims 1-83

1. (Withdrawn) A method of disinfecting article(s) that are susceptible to contamination by infectious prion protein, the method comprising the steps of:

   (a) heating said article(s) to a sufficient temperature and for sufficient time to enhance the proteolytic susceptibility of infective prion protein associated with said article(s); and

   (b) exposing the heated article(s) to a proteolytic enzyme that is effective for at least partial reduction of the infective protein prion associated with said article(s).

2. (Withdrawn) The method of claim 1, wherein said articles comprise surgical instruments.

3. (Withdrawn) The method of claim 2, wherein said surgical instrument(s) are selected from the group consisting of: clamps, forceps, scissors, knives, cables, punches, tweezers, cannulae, calipers, carvers, curettes, scalers, dilators, clip applicators, retractors, contractors, excavators, needle holders, suction tubes, trocars, coagulation electrodes, electroencephalographic depth electrodes, rib and sternum spreaders, bipolar probes, and rib shears.

4. (Withdrawn) The method of claim 1, wherein said article(s) comprise cutleries and kitchen utensils.

5. (Withdrawn) The method of claim 4, wherein said cutleries and kitchen utensils are selected from the group consisting of: knives, forks, scissors, peelers, parers, slicers, spatulas, and cleavers.

6. (Withdrawn) The method of claim 1, wherein said article(s) comprise laboratory apparatus(es).

7. (Withdrawn) The method of claim 6, wherein said laboratory apparatus(es) are selected from the group consisting of: containers, filtration devices, centrifuges, spectrophotometers, and fluorometers.

8. (Withdrawn) The method of claim 1, wherein said article(s) comprise veterinary devices.

9. (Withdrawn) The method of claim 8, wherein said veterinary devices are selected from the group consisting of clamps, forceps, knives, saws, probes, and electronic stun equipment.

10. (Withdrawn) The method of claim 1, wherein the temperature in step (a) comprises a temperature not exceeding about 150°C.

11. (Withdrawn) The method of claim 1, wherein the temperature in step (a) comprises a temperature of at least 35°C.

12. (Withdrawn) The method of claim 1, wherein the temperature in step (a) comprises a temperature below about 150°C.

13. (Withdrawn) The method of claim 1, wherein the temperature in step (a) comprises a temperature in a range of from about 100°C to about 150°C.

14. (Withdrawn) The method of claim 1, wherein the temperature in step (a) comprises a temperature in a range of from about 125°C to about 140°C.

15. (Withdrawn) The method of claim 1, wherein step (b) is conducted at lower temperature than step (a).

16. (Withdrawn) The method of claim 1, wherein step (b) is carried out at temperature above about 40°C.

17. (Withdrawn) The method of claim 1, wherein step (b) is carried out at temperature above about 50°C.

18. (Withdrawn) The method of claim 1, wherein step (b) is carried out at temperature in a range of from about 35°C to about 75°C.

19. (Withdrawn) The method of claim 1, wherein step (b) is carried out at temperature in a range of from about 40°C to about 75°C.

20. (Withdrawn) The method of claim 1, wherein step (b) is carried out at temperature in a range of from about 50°C to about 65°C.

21. (Withdrawn) The method of claim 1, wherein the proteolytic enzyme comprises at least one enzyme selected from the group consisting of keratinase enzymes, proteinase K, trypsins, chymotrypsins, pepsins, chymosins, cathepsins, subtilisins, elastases, collagenases, endopeptidases, peptidases, oligopeptidease, thermolysins, bacillolysin, mycilysins, carboxypeptidases, leucyl aminopeptidases, aminopeptidases, extremthermophilic proteases, carbonyl hydrolase, papain, pancreatin, streptokinase, streptodornase, ficin, carboxypeptidase, chymopapain, and bromelin.

22. (Withdrawn) The method of claim 1, wherein the proteolytic enzyme comprises a keratinase enzyme.

23. (Withdrawn) The method of claim 1, wherein the proteolytic enzyme comprises an active fragment of a keratinase enzyme.

24. (Withdrawn) The method of claim 1, wherein the proteolytic enzyme comprises a Bacillus licheniformis PWD-1 enzyme or an active fragment thereof.

25. (Withdrawn) The method of claim 1, wherein the proteolytic enzyme comprises a protease enzyme.

26. (Withdrawn) The method of claim 25, wherein the protease enzyme comprises a carbonyl hydrolase.

27. (Withdrawn) The method of claim 26, wherein the carbonyl hydrolase comprises subtilisin.

28. (Withdrawn) The method of claim 27, wherein the subtilisin comprises a mutant of wild-type Bacillus amyloliquefaciens subtilisin, comprising one or more amino acid substitutions, additions, or deletions.

29. (Withdrawn) The method of claim 25, wherein the protease enzyme comprises at least one enzyme selected from the group consisting of: papain, pancreatin, trypsin, chymotrypsin, pepsin, streptokinase, streptodornase, ficin, carboxypeptidase, aminopeptidase, chymopapain, bromelin, and subtilisin.

30. (Withdrawn) A method of removing infective prion protein from a surgical instrument contaminated with same, the method including (a) heating the surgical instrument at a temperature in a range of from about 100°C to about 150°C, followed by (b) exposing the heated surgical instrument to a proteolytic enzyme at a temperature in a range of from about 35°C to about 100°C at which the proteolytic enzyme is thermally stable and proteolytically effective to at least partially destroy the infective prion protein contaminating said surgical instrument.

31. (Withdrawn) The method of claim 30, wherein said heating is conducted for a time of from about 5 minutes to about 5 hours.

32. (Withdrawn) The method of claim 30, wherein the proteolytic enzyme comprises at least one enzyme selected from the group consisting of keratinase enzymes, proteinase K, trypsins,

chymotrypsins, pepsins, chymosins, cathepsins, subtilisins, elastases, collagenases, endopeptidases, peptidases, oligopeptidease, thermolysins, bacillolysin, mycilysins, carboxypeptidases, leucyl aminopeptidases, aminopeptidases, extremthermophilic proteases, carbonyl hydrolase, papain, pancreatin, streptokinase, streptodornase, ficin, carboxypeptidase, chymopapain, and bromelin.

33. (Withdrawn) The method of claim 30, wherein the proteolytic enzyme comprises *Bacillus licheniformis* PWD-1 keratinase.

34. (Withdrawn) The method of claim 1, wherein the proteolytic enzyme comprises a protease enzyme.

35. (Withdrawn) The method of claim 34, wherein the protease enzyme comprises a carbonyl hydrolase.

36. (Withdrawn) The method of claim 35, wherein the carbonyl hydrolase comprises subtilisin.

37. (Withdrawn) The method of claim 36 , wherein the subtilisin comprises a mutant of wild-type Bacillus amyloliquefaciens subtilisin, comprising one or more amino acid substitutions, additions, or deletions.

38. (Withdrawn) The method of claim 34, wherein the protease enzyme comprises at least one enzyme selected from the group consisting of: papain, pancreatin, trypsin, chymotrypsin, pepsin, streptokinase, streptodornase, ficin, carboxypeptidase, aminopeptidase, chymopapain, bromelin, and subtilisin.

39. (Previously presented) A system comprising:

(a) one or more articles susceptible to contamination by infectious prion protein;

(b) means for heating said articles;

(c) a proteolytic enzyme selected from the group consisting of keratinases and subtilisins; and

(d) means for exposing said articles to said proteolytic enzyme,

wherein said one or more articles are characterized by a first elevated temperature of at least 40°C and not more than about 150°C during a first duration, wherein said articles are characterized by a second elevated temperature in a range of from about 50°C to about 65°C and exposure to said proteolytic enzyme during a second, subsequent duration.

40. (Previously presented) The system of claim 39, wherein the proteolytic enzyme comprises keratinase.

41. (Previously presented) The system of claim 40, wherein the keratinase is provided in a solution at a concentration within a range of from about 0.2 g/L to about 1.0 g/L.

42. (Previously presented) The system of claim 41, wherein the solution comprises a solvent selected from the group consisting of distilled water, alcohol, buffer solution, and detergent solution.

43. (Previously presented) The system of claim 42, wherein said solution further comprises one or more chemical additives selected from the group consisting of surfactants, builders, boosters, and fillers.

44. (Previously presented) The system of claim 39, wherein said articles comprise surgical instruments.

45. (Previously presented) The system of claim 44, wherein said surgical instrument(s) are selected from the group consisting of: clamps, forceps, scissors, knives, cables, punches, tweezers, cannulae, calipers, carvers, curettes, scalers, dilators, clip applicators, retractors, contractors,

excavators, needle holders, suction tubes, trocars, coagulation electrodes, electroencephalographic depth electrodes, rib and sternum spreaders, bipolar probes, and rib shears.

46. (Previously presented) The system of claim 39, wherein said articles comprise cutleries and kitchen utensils.

47. (Previously presented) The system of claim 46, wherein said cutleries and kitchen utensils are selected from the group consisting of: knives, forks, scissors, peelers, parers, slicers, spatulas, and cleavers.

48. (Previously presented) The system of claim 47, wherein said laboratory apparatuses are selected from the group consisting of: containers, filtration devices, centrifuges, spectrophotometers, and fluorometers.

49. (Previously presented) The system of claim 39, wherein said article(s) comprise veterinary devices.

50. (Previously presented) The system of claim 49, wherein said veterinary devices are selected from the group consisting of clamps, forceps, knives, saws, probes, and electronic stun equipment.

51. (Previously presented) The system of claim 39, wherein said first elevated temperature is higher than said second elevated temperature.

52. (Cancelled).

53. (Previously presented) The system of claim 39, wherein said first elevated temperature is at least about 60°C.

54. (Previously presented) The system of claim 39, wherein said first elevated temperature is in a

range of from about 100°C to about 150°C.

55. (Previously presented) The system of claim 39, wherein said first elevated temperature is at least about 75°C.

56. (Previously presented) A system comprising:

(a) one or more articles susceptible to contamination by infectious prion protein;

(b) means for heating said one or more articles;

(c) a proteolytic enzyme selected from the group consisting of keratinases and subtilisins; and

(d) means for exposing said articles to said proteolytic enzyme;

wherein said one or more articles are characterized by an elevated temperature of from about 40°C to about 60°C and exposure to said proteolytic enzyme.

57-61. (Cancelled).

63. (Previously presented) The system of claim 39, wherein the proteolytic enzyme comprises a keratinase enzyme.

64-67. (Cancelled).

68. (Withdrawn) The system of claim 39, wherein the proteolytic enzyme comprises subtilisin.

69. (Withdrawn) The system of claim 68, wherein the subtilisin comprises a mutant of wild-type Bacillus amyloliquefaciens subtilisin, comprising one or more amino acid substitutions, additions, or deletions.

70. (Cancelled).

71. (Previously presented) A system comprising (a) a surgical instrument contaminated with infective prior protein; (b) means for heating the surgical instrument; (c) a proteolytic enzyme that is thermally stable at a temperature in a range of from about 35°C to about 100°C and proteolytically effective to at least partially destroy the infective prion protein contaminating said surgical instrument, and (d) means for exposing the surgical instrument to the proteolytic enzyme, wherein said surgical instrument is characterized by a first elevated temperature in a range of from about 100°C to about 150°C during a first duration, and wherein said surgical instrument is characterized by a second elevated temperature in a range of from about 35°C to about 100°C and exposure to said proteolytic enzyme during a second, subsequent duration.

72. (Cancelled).

73. (Previously presented) The system of claim 71, wherein the proteolytic enzyme comprises at least one enzyme selected from the group consisting of keratinase enzymes, proteinase K, trypsins, chymotrypsins, pepsins, chymosins, cathepsins, subtilisins, elastases, collagenases, endopeptidases, peptidases, oligopeptidease, thermolysins, bacillolysin, mycilysins, carboxypeptidases, leucyl aminopeptidases, aminopeptidases, extremthermophilic proteases, carbonyl hydrolase, papain, pancreatin, streptokinase, streptodornase, ficin, carboxypeptidase, chymopapain, and bromelin.

74. (Previously presented) The system of claim 71, wherein the proteolytic enzyme comprises *Bacillus licheniformis* PWD-1 keratinase.

75. (Withdrawn) The system of claim 71, wherein the proteolytic enzyme comprises a protease enzyme.

76. (Withdrawn) The system of claim 75, wherein the protease enzyme comprises a carbonyl hydrolase.

77. (Withdrawn) The system of claim 76, wherein the carbonyl hydrolase comprises subtilisin.

78. (Withdrawn) The system of claim 77, wherein the subtilisin comprises a mutant of wild-type Bacillus amyloliquefaciens subtilisin, comprising one or more amino acid substitutions, additions, or deletions.

79. (Withdrawn) The system of claim 75, wherein the protease enzyme comprises at least one enzyme selected from the group consisting of: papain, pancreatin, trypsin, chymotrypsin, pepsin, streptokinase, streptodornase, ficin, carboxypeptidase, aminopeptidase, chymopapain, bromelin, and subtilisin.

80. (Previously presented) A system comprising:

(a) one or more articles susceptible to contamination by infectious prion protein;

(b) means for heating said articles;

(c) *Bacillus licheniformis* PWD-1 keratinase; and

(d) means for exposing the heated articles to the *Bacillus licheniformis* PWD-1 keratinase,

wherein said articles are characterized by a first elevated temperature of at least 40°C and not more than about 150°C during a first duration, and wherein said articles are characterized by a second elevated temperature in a range of from about 50°C to about 65°C and exposure to the *Bacillus licheniformis* PWD-1 keratinase during a second, subsequent duration.

81. (Cancelled).

82. (Previously presented) A system comprising:

(a) one or more articles susceptible to contamination by infectious prion protein;

(b) means for heating said articles;

(c) *Bacillus licheniformis* PWD-1 keratinase; and

(d) means for exposing the articles to *Bacillus licheniformis* PWD-1 keratinase,

wherein said articles are characterized by an elevated temperature of from about 40°C to about 60°C and exposure to the *Bacillus licheniformis* PWD-1 keratinase.

83. (Cancelled).

EVIDENCE APPENDIX

Statement of Evidence

Applicant submitted the enclosed Affidavit under 37 CFR §1.32 on April 16, 2004 and the Examiner entered this Affidavit by June 30, 2004.

Copies of the following references were relied on by Examiner and are included herewith:

(a) WHO Infection Control Guidelines for Transmissible Spongiform Encephalopathies: Report of a WHO Consultation, WORLD HEALTH ORGANIZATION (WHO), March 23-26, 1999 (hereinafter "WHO Document");

(f) **Bolton** et al., Molecular Characteristics of the Major Scrapie Prion Protein (hereinafter "Bolton"); and

(g) **Oesch** et al. Properties of the Scrapie Prion Protein: Quantitative Analysis of Protease Resistance (hereinafter "Oesch").

All U.S. Patents have not been included because of easy access to same in the USPTO